## JUL 0 9 2008 W

## SEQUENCE LISTING

Chan, Doug W Chen, Ping-Chi B Chen, David J

<120> DNA Dependent Protein Kinase Catalytic Subunit Phosphorylation Sites and Antibodies Thereto

<130> IB-1807 PCT

<140> US 10/511,561

<141> 2004-10-15

<150> US 60/375,094

<151> 2002-04-22

<160> 28

<170> PatentIn version 3.1

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Cys Arg Glu Glu Ile Leu Lys Phe Leu Cys Ile Phe Leu Glu Lys Met 85 90 95

Gly Gln Lys Ile Ala Pro Tyr Ser Val Glu Ile Lys Asn Thr Cys Thr 100 105 110

Ser Val Tyr Thr Lys Asp Arg Ala Ala Lys Cys Lys Ile Pro Ala Leu 115 120 125

Asp Leu Leu Ile Lys Leu Leu Gln Thr Phe Arg Ser Ser Arg Leu Met 130 135 140

Asp Glu Phe Lys Ile Gly Glu Leu Phe Ser Lys Phe Tyr Gly Glu Leu 145 150 155 160

Ala Leu Lys Lys Lys Ile Pro Asp Thr Val Leu Glu Lys Val Tyr Glu 165 170 175

Leu Leu Gly Leu Gly Glu Val His Pro Ser Glu Met Ile Asn Asn 180 185 190

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Lys 225	Gly	Leu	Ser	Ser	Leu 230	Leu	Cys	Asn	Phe	Thr 235	Lys	Ser	Met	Glu	Glu 240
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Tyr	Ser 450	Pro	Lys	Met	Gln	Leu 455	Val	Cys	Cys	Arg	Ala 460	Ile	Val	Lys	Val
Phe 465	Leu	Ala	Leu	Ala	Ala 470	Lys	Gly	Pro	Val	Leu 475	Arg	Asn	Cys	Ile	Ser 480
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- Ala Thr Gln Met Pro Glu Gly Gly Gln Gly Ala Pro Pro Met Tyr Gln 945 950 955 960
- Leu Tyr Lys Arg Thr Phe Pro Val Leu Leu Arg Leu Ala Cys Asp Val 965 970 975
- Asp Gln Val Thr Arg Gln Leu Tyr Glu Pro Leu Val Met Gln Leu Ile 980 985 990
- His Trp Phe Thr Asn Asn Lys Lys Phe Glu Ser Gln Asp Thr Val Ser 995 1000 1005
- Leu Leu Glu Ala Ile Leu Asp Gly Ile Val Asp Pro Val Asp Ser 1010 1015 1020
- Thr Leu Arg Asp Phe Cys Gly Arg Cys Ile Arg Glu Phe Leu Lys 1025 1030 1035
- Trp Ser Ile Lys Gln Ile Thr Pro Gln Gln Gln Glu Lys Ser Pro 1040 1045 1050
- Val Asn Thr Lys Ser Leu Phe Lys Arg Leu Tyr Ser Leu Ala Leu 1055 1060 1065
- His Pro Asn Ala Phe Lys Arg Leu Gly Ala Ser Leu Ala Phe Asn 1070 1075 1080
- Asn Ile Tyr Arg Glu Phe Arg Glu Glu Glu Ser Leu Val Glu Gln 1085 1090 1095
- Phe Val Phe Glu Ala Leu Val Ile Tyr Met Glu Ser Leu Ala Leu 1100 1105 1110
- Ala His Ala Asp Glu Lys Ser Leu Gly Thr Ile Gln Gln Cys Cys 1115 1120 1125
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- Ser Leu Asn Lys Ala Lys Lys Arg Arg Leu Pro Arg Gly Phe Pro 1145 1150 1155.

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Val	Arg 1340	Ile	Met	Glu	Phe	Thr 1345	Thr	Thr	Leu	Leu	Asn 1350	Thr	Ser	Pro
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	1775					Ser 1780					1785			
	1790					Val 1795					1800		-	
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1835 1840 1845

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Cys	Glu 2585	Phe	Gln	Glu	Tyr	Thr 2590	Ile	Asp	Ser	Asp	Trp 2595	Arg	Phe	Arg
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Arg	Leu 2900	Leu	Pro	Ala	Glu	Leu 2905	Pro	Ala	Lys	Arg	Val 2910	_	Gly	Lys
Ala	Arg 2915	Leu	Pro	Pro	Asp	Val 2920	Leu	Arg	Trp	Val	Glu 2925	Leu	Ala	Lys
Leu	Tyr 2930	Arg	Ser	Ile	Gly	Glu 2935	Tyr	Asp	Val	Leu	Arg 2940	Gly	Ile	Phe
Thr	Ser 2945	Glu	Ile	Gly	Thr	Lys 2950	Gln	Ile	Thr	Gln	Ser 2955	Ala	Leu	Leu
Ala	Glu 2960	Ala	Arg	Ser	Asp	Tyr 2965	Ser	Glu	Āla	Ala	Lys 2970	Gln	Tyr	Asp
Glu	Ala 2975	Leu	Asn	Lys	Gln	Asp 2980	Trp	Val	Asp	Gly	Glu 2985	Pro	Thr	Glu

Ala Glu Lys Asp Phe Trp Glu Leu Ala Ser Leu Asp Cys Tyr Asn His Leu Ala Glu Trp Lys Ser Leu Glu Tyr Cys Ser Thr Ala Ser Ile Asp Ser Glu Asn Pro Pro Asp Leu Asn Lys Ile Trp Ser Glu Pro Phe Tyr Gln Glu Thr Tyr Leu Pro Tyr Met Ile Arg Ser Lys Leu Lys Leu Leu Gln Gly Glu Ala Asp Gln Ser Leu Leu Thr Phe Ile Asp Lys Ala Met His Gly Glu Leu Gln Lys Ala Ile Leu Glu Leu His Tyr Ser Gln Glu Leu Ser Leu Leu Tyr Leu Leu Gln Asp Asp Val Asp Arg Ala Lys Tyr Tyr Ile Gln Asn Gly Ile Gln Ser Phe Met Gln Asn Tyr Ser Ser Ile Asp Val Leu Leu His Gln Ser Arg Leu Thr Lys Leu Gln Ser Val Gln Ala Leu Thr Glu Ile Gln Glu Phe Ile Ser Phe Ile Ser Lys Gln Gly Asn Leu Ser Ser Gln Val Pro Leu Lys Arg Leu Leu Asn Thr Trp Thr Asn Arg Tyr Pro Asp Ala Lys Met Asp Pro Met Asn Ile Trp Asp Asp Ile Ile Thr Asn Arg Cys Phe Phe Leu Ser Lys Ile Glu Glu Lys Leu Thr Pro Leu Pro Glu Asp Asn Ser Met Asn Val Asp Gln Asp Gly Asp

3205 3210

Pro	Ser 3215	Asp	Arg	Met	Glu	Val 3220	Gln	Glu	Gln	Glu	Glu 3225	Asp	Ile	Ser
Ser	Leu 3230	Ile	Arg	Ser	Cys	Lys 3235		Ser	Met	Lys	Met 3240	Lys	Met	Ile
Asp	Ser 3245	Ala	Arg	Lys	Gln	Asn 3250	Asn	Phe	Ser	Leu	Ala 3255	Met	Lys	Leu
Leu	Lys 3260	Glu	Leu	His	Lys	Glu 3265		Lys	Thr	Arg	Asp 3270	Asp	Trp	Leu
Val	Ser 3275	Trp	Val	Gln	Ser	Tyr 3280	Cys	Arg	Leu	Ser	His 3285	Cys	Arg	Ser
Arg	Ser 3290	Gln	Gly	Cys	Ser	Glu 3295	Gln	Val	Leu	Thr	Val 3300	Leu	Lys	Thr
Val	Ser 3305	Leu	Leu	Asp	Glu	Asn 3310	Asn	Val	Ser	Ser	Tyr 3315	Leu	Ser	Lys
Asn	Ile 3320	Leu	Ala	Phe	Arg	Asp 3325	Gln	Asn	Ile	Leu	Leu 3330	Gly	Thr	Thr
Tyr	Arg 3335	Ile	Ile	Ala	Asn	Ala 3340	Leu	Ser	Ser	Glu	Pro 3345	Ala	Cys	Leu
Ala	Glu 3350	Ile	Glu	Glu	Asp	Lys 3355	Ala	Arg	Arg	Ile	Leu 3360	Glu	Leu	Ser
Gly	Ser 3365	Ser	Ser	Glu	Asp	Ser 3370		Lys	Val	Ile	Ala 3375	Gly	Leu	Tyr
Gln	Arg 3380	Ala	Phe	Gln	His	Leu 3385	Ser	Glu	Ala	Val	Gln 3390	Ala	Ala	Glu
Glu	Glu 3395	Ala	Gln	Pro	Pro	Ser 3400	Trp	Ser	Cys	Gly	Pro 3405	Ala	Ala	Gly
Val	Ile 3410	Asp	Ala	Tyr	Met	Thr 3415	Leu	Ala	Asp	Phe	Cys 3420	Asp	Gln	Gln
Leu	Arg 3425	Lys	Glu	Glu	Glu	Asn 3430	Ala	Ser	Val	Thr	Asp 3435	Ser	Ala	Glu

Leu	Gln 3440		Tyr	Pro	Ala	Leu 3445	Val	Val	Glu	Lys	Met 3450	Leu	Lys	Ala
Leu	Lys 3455	Leu	Asn	Ser	Asn	Glu 3460	Ala	Arg	Leu	Lys	Phe 3465		Arg	Leu
Leu	Gln 3470		Ile	Glu	Arg	Tyr 3475		Glu	Glu	Thr	Leu 3480		Leu	Met
Thr	Lys 3485	Glu	Ile	Ser	Ser	Val 3490	Pro	Cys	Trp	Gln	Phe 3495	Ile	Ser	Trp
Ile	Ser 3500	His	Met	Val	Ala	Leu 3505	Leu	Asp	Lys	Asp	Gln 3510		Val	Ala
Val	Gln 3515	His	Ser	Val	Glu	Glu 3520	Ile	Thr	Asp	Asn	Tyr 3525	Pro	Gln	Ala
Ile	Val 3530	Tyr	Pro	Phe	Ile	Ile 3535	Ser	Ser	Glu	Ser	Tyr 3540	Ser	Phe	Lys
Asp ,	Thr 3545	Ser	Thr	Gly	His	Lys 3550	Asn	Lys	Glu	Phe	Val 3555		Arg	Ile
Lys	Ser 3560	Lys	Leu	Asp	Gln	Gly 3565	Gly	Val	Ile	Gln	Asp 3570	Phe	Ile	Asn
Ala	Leu 3575	Asp	Gln	Leu	Ser	Asn 3580	Pro	Glu	Leu	Leu	Phe 3585	Lys	Asp	Trp
Ser	Asn 3590	Asp	Val	Arg	Ala	Glu 3595	Leu	Ala	Lys	Thr	Pro 3600	Val	Asn	Lys
Lys	Asn 3605	Ile	Glu	Lys	Met	Tyr 3610	Glu	Arg	Met	Tyr	Ala 3615	Ala	Leu	Gly
Asp	Pro 3620	Lys	Ala	Pro	Gly	Leu 3625	Gly	Ala	Phe	Arg	Arg 3630	Lys	Phe	Ile
Gln	Thr 3635	Phe	Gly	Lys	Glu	Phe 3640	Asp	Lys	His	Phe	Gly 3645	_	Gly	Gly
Ser	Lys 3650	Leu	Leu	Arg	Met	Lys 3655	Leu	Ser	Asp	Phe	Asn 3660	Asp	Ile	Thr

Asn Met Leu Leu Lys Met Asn Lys Asp Ser Lys Pro Pro Gly

3665 3670 3675

Asn	Leu 3680	Lys	Glu	Cys	Ser	Pro 3685	Trp	Met	Ser	Asp	Phe 3690	Lys	Val	Glu
Phe	Leu 3695	Arg	Asn	Glu	Leu	Glu 3700	Ile	Pro	Gly	Gln	Tyr 3705	Asp	Gly	Arg
Gly	Lys 3710	Pro	Leu	Pro	Glu	Tyr 3715	His	Val	Arg	Ile	Ala 3720	Gly	Phe	Asp
Glu	Arg 3725	Val	Thr	Val	Met	Ala 3730		Leu	Arg	Arg	Pro 3735	Lys	Arg	Ile
Ile	Ile 3740	Arg	Gly	His	Asp	Glu 3745	Arg	Glu	His	Pro	Phe 3750	Leu	Val	Lys
Gly	Gly 3755	Glu	Asp	Leu	Arg	Gln 3760	Asp	Gln	Arg	Val	Glu 3765	Gln	Leu	Phe
Gln	Val 3770	Met	Asn	Gly	Ile	Leu 3775	Ala	Gln	Asp	Ser	Ala 3780	Cys	Ser	Gln
Arg	Ala 3785	Leu	Gln	Leu	Arg	Thr 3790	Tyr	Ser	Val	Val	Pro 3795	Met	Thr	Ser
Arg	Leu 3800	Gly	Leu	Ile	Glu	Trp 3805	Leu	Glu	Asn	Thr	Val 3810	Thr	Leu	Lys
Asp	Leu 3815	Leu	Leu	Asn	Thr	Met 3820	Ser	Gln	Glu	Glu	Lys 3825	Ala	Ala	Tyr
Leu	Ser 3830	Asp	Pro	Arg	Ala	Pro 3835	Pro	Cys	Glu	Tyr	Lys 3840	Asp	Trp	Leu
Thr	Lys 3845	Met	Ser	Gly	Lys	His 3850	Asp	Val	Gly	Ala	Tyr 3855	Met	Leu	Met
Tyr	Lys 3860	Gly	Ala	Asn	Arg	Thr 3865	Glu	Thr	Val	Thr	Ser 3870	Phe	Arg	Lys
Arg	Glu 3875	Ser	Lys	Val	Pro	Ala 3880	Asp	Leu	Leu	Lys	Arg 3885	Ala	Phe	Val
Arg	Met 3890	Ser	Thr	Ser	Pro	Glu 3895	Ala	Phe	Leu	Ala	Leu 3900	Arg	Ser	His

Phe	Ala 3905		Ser	His	Ala	Leu 3910		Cys	Ile	Ser	His 3915	Trp	Ile	Leu
Gly	Ile 3920		Asp	Arg	His	Leu 3925		Asn	Phe	Met	Val 3930		Met	Glu
Thr	Gly 3935	Gly	Val	Ile	Gly	Ile 3940	Asp	Phe	Gly	His	Ala 3945	Phe	Gly	Ser
Ala	Thr 3950		Phe	Leu	Pro	Val 3955	Pro	Glu	Leu	Met	Pro 3960	Phe	Arg	Leu
Thr	Arg 3965	Gln	Phe	Ile	Asn	Leu 3970	Met	Leu	Pro	Met	Lys 3975	Glu	Thr	Gly
Leu	Met 3980		Ser	Ile	Met	Val 3985	His	Ala	Leu	Arg	Ala 3990	Phe	Arg	Ser
Asp	Pro 3995	Gly	Leu	Leu	Thr	Asn 4000	Thr	Met	Asp	Val	Phe 4005	Val	Lys	Glu
Pro	Ser 4010	Phe	Asp	Trp	Lys	Asn 4015	Phe	Glu	Gln	Lys	Met 4020	Leu	Lys	Lys
Gly	Gly 4025	Ser	Trp	Ile	Gln	Glu 4030	Ile	Asn	Val	Ala	Glu 4035	Lys	Asn	Trp
Tyr	Pro 4040	Arg	Gln	Lys	Ile	Cys 4045	Tyr	Ala	Lys	Arg	Lys 4050	Leu	Ala	Gly
Ala	Asn 4055	Pro	Ala	Val	Ile	Thr 4060	Cys	Asp	Glu	Leu	Leu 4065	Leu	Gly	His
Glu	Lys 4070	Ala	Pro	Ala	Phe	Arg 4075	Asp	Tyr	Val	Ala	Val 4080	Ala	Arg	Gly
Ser	Lys 4085	Asp	His	Asn	Ile	Arg 4090	Ala	Gln	Glu	Pro	Glu 4095	Ser	Gly	Leu
Ser	Glu 4100	Glu	Thr	Gln	Val	Lys 4105	Cys	Leu	Met	Asp	Gln 4110	.Ala	Thr	Asp
Pro	Asn 4115	Ile	Leu	Gly	Arg	Thr 4120	Trp	Glu	Gly	Trp	Glu 4125	Pro	Trp	Met

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<221> PEPTIDE
<222> (1)..(21)
<223> HUMAN GENETIC ORIGIN
<220>
<221> MOD RES
<222> (11)..(11)
<223> PHOSPHORYLATION at T2609
<400> 4
Ser Thr Val Leu Thr Pro Met Phe Val Glu Thr Gln Ala Ser Gln Gly
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                                   10
Thr Leu Gln Thr Arg
           20
<210> 5
<211> 29
<212> PRT
<213> Artificial Sequence
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<221> PEPTIDE
<222> (1)..(29)
<223> HUMAN GENETIC ORIGIN
<220>
<221> MOD RES
<222> (13)..(13)
<223> PHOSPHORYLATION at S2056
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Asp Phe Ser Thr Gly Val Gln Ser Tyr Ser Tyr Ser Ser Gln Asp Pro
               5
                                   10
Arg Pro Ala Thr Gly Arg Phe Arg Arg Glu Gln Arg
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<211> 303
<212> PRT
<213> Artificial Sequence
<220>
<221> PEPTIDE
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<210> 4

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Arg Asp Pro Thr Val His Asp Asp Val Leu Glu Leu Glu Met Asp Glu

200 205

Leu Asn Arg His Glu Cys Met Ala Pro Leu Thr Ala Leu Val Lys His Met His Arg Ser Leu Gly Pro Pro Gln Gly Glu Glu Asp Ser Val Pro 230 235 Arg Asp Leu Pro Ser Trp Met Lys Phe Leu His Gly Lys Leu Gly Asn 245 250 Pro Ile Val Pro Leu Asn Ile Arg Leu Phe Leu Ala Lys Leu Val Ile 260 265 270 Asn Thr Glu Glu Val Phe Arg Pro Tyr Ala Lys His Trp Leu Ser Pro 275 285 Leu Leu Gln Leu Ala Ala Ser Glu Asn Asn Gly Gly Glu Gly Ile <210> 7 <211> 388 <212> PRT <213> Artificial Sequence <220> <221> PEPTIDE <222> (1)..(388) <223> HUMAN GENETIC ORIGIN <220> <221> MOD RES <222> (177)..(177) <223> PHOSPHORYLATION at S2056 <400> 7 Met Tyr Ser Arg Leu Pro Lys Asp Asp Val His Ala Lys Glu Ser Lys 5 15 Ile Asn Gln Val Phe His Gly Ser Cys Ile Thr Glu Gly Asn Glu Leu 20 25 30 Thr Lys Thr Leu Ile Lys Leu Cys Tyr Asp Ala Phe Thr Glu Asn Met Ala Gly Glu Asn Gln Leu Leu Glu Arg Arg Leu Tyr His Cys Ala

Ala Tyr Asn Cys Ala Ile Ser Val Ile Cys Cys Val Phe Asn Glu Leu

75

Lys	Phe	Tyr	Gln	Gly 85	Phe	Leu	Phe	Ser	Glu 90	Lys	Pro	Glu	Lys	Asn 95	Leu
Leu	Ile	Phe	Glu 100	Asn	Leu	Ile	Asp	Leu 105	Lys	Arg	Arg	Tyr	Asn 110	Phe	Pro
Val	Glu	Val 115	Glu	Val	Pro	Met	Glu 120	Arg	Lys	Lys	Lys	Tyr 125	Ile	Glu	Ile
Arg	Lys 130	Glu	Ala	Arg	Glu	Ala 135	Ala	Asn	Gly	Asp	Ser 140	Asp	Gly	Pro	Ser
Tyr 145	Met	Ser	Ser	Leu	Ser 150	Tyr	Leu	Ala	Asp	Ser 155	Thr	Leu	Ser	Glu	Glu 160
Met	Ser	Gln	Phe	Asp 165	Phe	Ser	Thr	Gly	Val 170	Gln	Ser	Tyr	Ser	Tyr 175	Ser
Ser	Gln	Asp	Pro 180	Arg	Pro	Ala	Thr	Gly 185	Arg	Phe	Arg	Arg	Arg 190	Glu	Gln
Arg	Asp	Pro 195	Thr	Val	His	Asp	Asp 200	·Val	Leu	Glu	Leu	Glu 205	Met	Asp	Glu
Leu	Asn 210	Arg	His	Glu	Cys	Met 215	Ala	Pro	Leu	Thr	Ala 220	Leu	Val	Lys	His
Met 225	His	Arg	Ser	Leu	Gly 230	Pro	Pro	Gln	Gly	Glu 235	Glu	Asp	Ser	Val	Pro 240
Arg	Asp	Leu	Pro	Ser 245	Trp	Met	Lys	Phe	Leu 250	His	Gly	Lys	Leu	Gly 255	Asn
Pro	Ile	Val	Pro 260	Leu	Asn	Ile	Arg	Leu 265	Phe	Leu	Ala	Lys	Leu 270	Val	Ile
Asn	Thr	Glu 275	Glu	Val	Phe	Arg	Pro 280	Tyr	Ala	Lys	His	Trp 285	Leu	Ser	Pro
Leu	Leu 290	Gln	Leu	Ala	Ala	Ser 295	Glu	Asn	Asn	Gly	Gly 300	Glu	Gly	Ile	His
Tyr 305	Met	Val	Val	Glu	Ile 310	Val	Ala	Thr	Ile	Leu 315	Ser	Trp	Thr	Gly	Leu 320

Ala Thr Pro Thr Gly Val Pro Lys Asp Glu Val Leu Ala Asn Arg Leu 325 330 Leu Asn Phe Leu Met Lys His Val Phe His Pro Lys Arg Ala Val Phe 345 Arg His Asn Leu Glu Ile Ile Lys Thr Leu Val Glu Cys Trp Lys Asp 355 360 365 Cys Leu Ser Ile Pro Tyr Arg Leu Ile Phe Glu Lys Phe Ser Gly Lys 370 375 380 Asp Pro Asn Ser 385 <210> 8 <211> 821 <212> PRT <213> Artificial Sequence <220> <221> PEPTIDE <222> (1)..(821) <223> HUMAN GENETIC ORIGIN <220> <221> MOD RES <222> (177)..(177) <223> PHOSPHORYLATION at S2056 <220> <221> MOD RES <222> (730)..(730) <223> PHOSPHORYLATION at T2609 <400> 8 Met Tyr Ser Arg Leu Pro Lys Asp Val His Ala Lys Glu Ser Lys 10 Ile Asn Gln Val Phe His Gly Ser Cys Ile Thr Glu Gly Asn Glu Leu 20 25

Ala Tyr Asn Cys Ala Ile Ser Val Ile Cys Cys Val Phe Asn Glu Leu

Thr Lys Thr Leu Ile Lys Leu Cys Tyr Asp Ala Phe Thr Glu Asn Met

Ala Gly Glu Asn Gln Leu Leu Glu Arg Arg Leu Tyr His Cys Ala

55

35

Lys Phe Tyr Gln Gly Phe Leu Phe Ser Glu Lys Pro Glu Lys Asn Leu 85 90 95

65

Leu Ile Phe Glu Asn Leu Ile Asp Leu Lys Arg Arg Tyr Asn Phe Pro  $100 \hspace{1.5cm} 105 \hspace{1.5cm} 110 \hspace{1.5cm}$ 

Val Glu Val Glu Val Pro Met Glu Arg Lys Lys Tyr Ile Glu Ile 115 120 125

Arg Lys Glu Ala Arg Glu Ala Ala Asn Gly Asp Ser Asp Gly Pro Ser 130 135 140

Tyr Met Ser Ser Leu Ser Tyr Leu Ala Asp Ser Thr Leu Ser Glu Glu 145 150 155 160

Met Ser Gln Phe Asp Phe Ser Thr Gly Val Gln Ser Tyr Ser Tyr Ser 165 170 175

Ser Gln Asp Pro Arg Pro Ala Thr Gly Arg Phe Arg Arg Glu Gln 180 185 190

Arg Asp Pro Thr Val His Asp Asp Val Leu Glu Leu Glu Met Asp Glu
195 200 205

Leu Asn Arg His Glu Cys Met Ala Pro Leu Thr Ala Leu Val Lys His 210 215 220

Met His Arg Ser Leu Gly Pro Pro Gln Gly Glu Glu Asp Ser Val Pro 225 230 235 240

Arg Asp Leu Pro Ser Trp Met Lys Phe Leu His Gly Lys Leu Gly Asn 245 250 255

Pro Ile Val Pro Leu Asn Ile Arg Leu Phe Leu Ala Lys Leu Val Ile 260 265 270

Asn Thr Glu Glu Val Phe Arg Pro Tyr Ala Lys His Trp Leu Ser Pro 275 280 285

Leu Leu Gln Leu Ala Ala Ser Glu Asn Asn Gly Gly Glu Gly Ile His 290 295 300

Tyr Met Val Val Glu Ile Val Ala Thr Ile Leu Ser Trp Thr Gly Leu 305 310 315 320

Ala	Thr	Pro	Thr	Gly 325	Val	Pro	Lys	Asp	Glu 330	Val	Leu	Ala	Asn	Arg 335	Leu
Leu	Asn	Phe	Leu 340	Met	Lys	His	Val	Phe 345	His	Pro	Lys	Arg	Ala 350	Val	Phe
Arg	His	Asn 355	Leu	Glu	Ile	Ile	Lys 360	Thr	Leu	Val	Glu	Cys 365	Trp	Lys	Asp
Cys	Leu 370	Ser	Ile	Pro	Tyr	Arg 375	Leu	Ile	Phe	Glu	Lys 380	Phe	Ser	Gly	Lys
Asp 385	Pro	Asn	Ser	Lys	Asp 390	Asn	Ser	Val	Gly	Ile 395	Gln	Leu	Leu	Gly	Ile 400
Val	Met	Ala	Asn	Asp 405	Leu	Pro	Pro	Tyr	Asp 410	Pro	Gln	Cys	Gly	Ile 415	Gln
Ser	Ser	Glu	Tyr 420	Phe	Gln	Ala	Leu	Val 425	Asn	Asn	Met	Ser	Phe 430	Val	Arg
Tyr	Lys	Glu 435	Val	Tyr	Ala	Ala	Ala 440	Ala	Glu	Val	Leu	Gly 445	Leu	Ile	Leu
Arg	Tyr 450	Val	Met	Glu	Arg	Lys 455	Asn	Ile	Leu	Glu	Glu 460	Ser	Leu	Cys	Glu
Leu 465	Val	Ala	Lys	Gln	Leu 470	Lys	Gln	His	Gln	Asn 475	Thr	Met	Glu	Asp	Lys 480
Phe	Ile	Val	Cys	Leu 485	Asn	Lys	Val	Thr	Lys 490	Ser	Phe	Pro	Pro	Leu 495	Ala
Asp	Arg	Phe	Met 500	Asn	Ala	Val	Phe	Phe 505	Leu	Leu	Pro	Lys	Phe 510	His	Gly
Val	Leu	Lys 515	Thr	Leu	Cys	Leu	Glu 520	Val	Val	Leu	Cys	Arg 525	Val	Glu	Gly
Met	Thr 530	Glu	Leu	Tyr	Phe	Gln 535	Leu	Lys	Ser	Lys	Asp 540	Phe	Val	Gln	Val
Met	Arg	His	Arg	Asp	Asp	Glu	Arg	Gln	Lys	Val	Cys	Leu	Asp	Ile	Ile
545					550					555					560

Tyr	Lys	Met	Met	Pro 565	Lys	Leu	Lys	Pro	Val 570	Glu	Leu	Arg	Glu	Leu 575	Leu
Asn	Pro	Val	Val 580	Glu	Phe	Val	Ser	His 585	Pro	Ser	Thr	Thr	Cys 590	Arg	Glu
Gln	Met	Tyr 595	Asn	Ile	Leu	Met	Trp 600	Ile	His	Asp	Asn	Tyr. 605	Arg	Asp	Pro
Glu	Ser 610	Glu	Thr	Asp	Asn 、	Asp 615	Ser	Gln	Glu	Ile	Phe 620	Lys	Leu	Ala	Lys
Asp 625	Val	Leu	Ile	Gln	Gly 630	Leu	Ile	Asp	Glu	Asn 635	Pro	Gly	Leu	Gln	Leu 640
Ile	Ile	Arg	Asn	Phe 645	Trp	Ser	His	Glu	Thr 650	Arg	Leu	Pro	Ser	Asn 655	Thr
Leu	Asp	Arg	Leu 660	Leu	Ala	Leu	Asn	Ser 665	Leu	Tyr	Ser	Pro	Lys 670	Ile	Glu
Val	His	Phe 675	Leu	Ser	Leu	Ala	Thr 680	Asn	Phe	Leu	Leu	Glu 685	Met	Thr	Ser
Met	Ser 690	Pro	Asp	Tyr	Pro	Asn 695	Pro	Met	Phe	Glu	His 700	Pro	Leu	Ser	Glu
Cys 705	Glu	Phe	Gln	Glu	Tyr 710	Thr	Ile	Asp	Ser	Asp 715	Trp	Arg	Phe	Arg	Ser 720
Thr	Val	Leu	Thr	Pro 725	Met	Phe	Val	Glu	Thr 730	Gln	Ala	Ser	Gln	Gly 735	Thr
Leu	Gln	Thr	Arg 740	Thr	Gln	Glu	Gly	Ser 745	Leu	Ser	Ala	Arg	Trp 750	Pro	Val
Ala	Gly	Gln 755	Ile	Arg	Ala	Thr	Gln 760	Gln	Gln	His	Asp	Phe 765	Thr	Leu	Thr
Gln	Thr 770	Ala	Asp	Gly	Arg	Ser 775	Ser	Phe	Asp	Trp	Leu 780	Thr	Gly	Ser	Ser
Thr 785	Asp	Pro	Leu	Val	Asp 790	His	Thr	Ser	Pro	Ser 795	Ser	Asp	Ser	Leu	Leu 800

Phe Ala His Lys Arg Ser Glu Arg Leu Gln Arg Ala Pro Leu Lys Ser 805 810 815

Val Gly Pro Asp Phe 820

<210> 9

<211> 440

<212> PRT

<213> Artificial Sequence

·<220>

<221> PEPTIDE

<222> (1)..(440)

<223> HUMAN GENETIC ORIGIN

<220>

<221> MOD RES

<222> (349)..(349)

<223> PHOSPHORYLATION at T2609

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Ser Gly Lys Asp Pro Asn Ser Lys Asp Asn Ser Val Gly Ile Gln Leu 1 5 10 15

Leu Gly Ile Val Met Ala Asn Asp Leu Pro Pro Tyr Asp Pro Gln Cys
20 25 30

Gly Ile Gln Ser Ser Glu Tyr Phe Gln Ala Leu Val Asn Asn Met Ser 35 40 45

Phe Val Arg Tyr Lys Glu Val Tyr Ala Ala Ala Ala Glu Val Leu Gly 50 60

Leu Ile Leu Arg Tyr Val Met Glu Arg Lys Asn Ile Leu Glu Glu Ser 65 70 75 80

Leu Cys Glu Leu Val Ala Lys Gln Leu Lys Gln His Gln Asn Thr Met 85 90 95

Glu Asp Lys Phe Ile Val Cys Leu Asn Lys Val Thr Lys Ser Phe Pro  $100 \hspace{1cm} 105 \hspace{1cm} 110$ 

Pro Leu Ala Asp Arg Phe Met Asn Ala Val Phe Phe Leu Leu Pro Lys 115 120 125

Phe His Gly Val Leu Lys Thr Leu Cys Leu Glu Val Val Leu Cys Arg 130 135 140

Val 145	Glu	Gly	Met	Thr	Glu 150	Leu	Tyr	Phe	Gln	Leu 155	Lys	Ser	Lys	Asp	Phe 160
Val	Gln	Val	Met	Arg 165	His	Arg	Asp	Asp	Glu 170	Arg	Gln	Lys	Val	Cys 175	Leu
Asp	Ile	Ile	Tyr 180	Lys	Met	Met	Pro	Lys 185	Leu	Lys	Pro		Glu 190	Leu	Arg
Glu	Leu	Leu 195	Asn	Pro	Val	Val	Glu 200	Phe	Val	Ser	His	Pro 205	Ser	Thr	Thr
Cys	Arg 210	Glu	Gln	Met	Tyr	Asn 215	Ile	Leu	Met	Trp	Ile 220	His	Asp	Asn	Tyr
Arg 225	Asp	Pro	Glu	Ser	Glu 230	Thr	Asp	Asn	Asp	Ser 235	Gln	Glu	Ile	Phe	Lys 240
Leu	Ala	Lys	Asp	Val 245	Leu	Ile	Gln	Gly	Leu 250	Ile	Asp	Glu	Asn	Pro 255	Gly
Leu	Gln	Leu	Ile 260	Ile	Arg	Asn	Phe	Trp 265	Ser	His	Glu	Thr	Arg 270	Leu	Pro
Ser	Asn	Thr 275	Leu	Asp	Arg	Leu	Leu 280	Ala	Leu	Asn	Ser	Leu 285	Tyr	Ser	Pro
Lys	Ile 290	Glu	Val	His	Phe	Leu 295	Ser	Leu	Ala	Thr	Asn 300	Phe	Leu	Leu	Glu
Met 305	Thr	Ser	Met	Ser	Pro 310	Asp	Tyr	Pro	Asn	Pro 315	Met	Phe	Glu	His	Pro 320
Leu	Ser	Glu	Cys	Glu 325	Phe	Gln	Glu	Tyr	Thr 330	Ile	Asp	Ser	Asp	Trp 335	Arg
Phe	Arg	Ser	Thr 340	Val	Leu	Thr	Pro	Met 345	Phe	Val	Glu	Thr	Gln 350	Ala	Ser
Gln	Gly	Thr 355	Leu	Gln	Thr	Arg	Thr 360	Gln	Glu	Gly	Ser	Leu 365	Ser	Ala	Arg
Trp	Pro 370	Val	Ala	Gly	Gln	Ile 375	Arg	Ala	Thr	Gln	Gln 380	Gln	His	Asp	Phe

Thr Leu Thr Gln Thr Ala Asp Gly Arg Ser Ser Phe Asp Trp Leu Thr 390 395 Gly Ser Ser Thr Asp Pro Leu Val Asp His Thr Ser Pro Ser Ser Asp 405 410 Ser Leu Leu Phe Ala His Lys Arg Ser Glu Arg Leu Gln Arg Ala Pro 425 Leu Lys Ser Val Gly Pro Asp Phe 435 <210> 10 <211> 200 <212> PRT <213> Artificial Sequence <220> <221> PEPTIDE <222> (1)..(200) <223> HUMAN GENETIC ORIGIN <220> <221> MOD\_RES  $\langle 222 \rangle$  (109) ... (109)<223> PHOSPHORYLATION at T2609 <400> 10 Leu Ala Lys Asp Val Leu Ile Gln Gly Leu Ile Asp Glu Asn Pro Gly 5 Leu Gln Leu Ile Ile Arg Asn Phe Trp Ser His Glu Thr Arg Leu Pro 25 Ser Asn Thr Leu Asp Arg Leu Leu Ala Leu Asn Ser Leu Tyr Ser Pro 40 Lys Ile Glu Val His Phe Leu Ser Leu Ala Thr Asn Phe Leu Leu Glu 50 55 60 Met Thr Ser Met Ser Pro Asp Tyr Pro Asn Pro Met Phe Glu His Pro 65 70 Leu Ser Glu Cys Glu Phe Gln Glu Tyr Thr Ile Asp Ser Asp Trp Arg 95 85 90

Phe Arg Ser Thr Val Leu Thr Pro Met Phe Val Glu Thr Gln Ala Ser

105

110

Gln Gly Thr Leu Gln Thr Arg Thr Gln Glu Gly Ser Leu Ser Ala Arg 115 120 125

Trp Pro Val Ala Gly Gln Ile Arg Ala Thr Gln Gln His Asp Phe 130 135 140

Thr Leu Thr Gln Thr Ala Asp Gly Arg Ser Ser Phe Asp Trp Leu Thr 145 150 155 160

Gly Ser Ser Thr Asp Pro Leu Val Asp His Thr Ser Pro Ser Ser Asp 165 170 175

Ser Leu Leu Phe Ala His Lys Arg Ser Glu Arg Leu Gln Arg Ala Pro 180 185 190

Leu Lys Ser Val Gly Pro Asp Phe 195 200

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Leu Gly Leu Ile Leu Arg Tyr Val Met Glu Arg Lys Asn Ile Leu Glu 50 55 60

Glu Ser Leu Cys Glu Leu Val Ala Lys Gln Leu Lys Gln His Gln Asn 65 70 75 80

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Pro L	_	Phe 115	His	Gly	Val	Leu	Lys 120	Thr	Leu	Cys	Leu	Glu 125	Val	Val	Leu
Cys A	rg V 30	Jal	Glu	Gly	Met	Thr 135	Glu	Leu	Tyr	Phe	Gln 140	Leu	Lys	Ser	Lys
Asp P	he V	/al	Gln	Val	Met 150	Arg	His	Arg	Asp	Asp 155	Glu	Arg	Gln	Lys	Val 160
Cys L	eu P	Asp	Ile	Ile 165	Tyr	Lys	Met	Met	Pro 170	Lys	Leu	Lys	Pro	Val 175	Glu
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Thr T		Cys 195	Arg	Glu	Gln	Met	Tyr 200	Asn	Ile	Leu	Met	Trp 205	Ile	His	Asp
Asn T	yr <i>P</i> 10	Arg	Asp	Pro	Glu	Ser 215	Glu	Thr	Asp	Asn	Asp 220	Ser	Gln	Glu	Ile
Phe L 225	ys I	Leu	Ala	Lys	Asp 230	Val	Leu	Ile	Gln	Gly 235	Leu	Ile	Asp	Glu	Asn 240
Pro G	ly I	Leu	Gln	Leu 245	Ile	Ile	Arg	Asn	Phe 250	Trp	Ser	His	Glu	Thr 255	Arg
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Leu G 2	lu M 90	1et	Thr	Ser	Met	Ser 295	Pro	Asp	Tyr	Pro	Asn 300	Pro	Met	Phe	Glu
His P 305	ro I	Leu	Ser	Glu	Cys 310	Glu	Phe	Gln	Glu	Tyr 315	Thr	Ile	Asp	Ser	Asp 320

Trp Arg Phe Arg Ser Thr Val Leu Thr Pro Met Phe Val Glu Thr Gln 330 Ala Ser Gln Gly Thr Leu Gln Thr Arg Thr Gln Glu Gly Ser Leu Ser 340 345 Ala Arg Trp Pro Val Ala Gly Gln Ile Arg Ala Thr Gln Gln His 360 365 Asp Phe Thr Leu Thr Gln Thr Ala Asp Gly Arg Ser Ser Phe Asp Trp 370 375 Leu Thr Gly Ser Ser Thr Asp Pro Leu Val Asp His Thr Ser Pro Ser 395 Ser Asp Ser Leu Leu Phe Ala His Lys Arg Ser Glu Arg Leu Gln Arg 410 Ala Pro Leu Lys Ser Val Gly Pro Asp Phe Gly Lys 420 425 <210> 12 <211> 273 <212> PRT <213> Artificial Sequence <220> <221> PEPTIDE <222> (1)..(273) <223> HUMAN GENETIC ORIGIN <220> <221> MOD\_RES  $\langle 222 \rangle$   $(180) \dots (180)$ <223> PHOSPHORYLATION at T2609 <400> 12 Glu Arg Gln Lys Val Cys Leu Asp Ile Ile Tyr Lys Met Met Pro Lys 5 10 Leu Lys Pro Val Glu Leu Arg Glu Leu Leu Asn Pro Val Val Glu Phe Val Ser His Pro Ser Thr Thr Cys Arg Glu Gln Met Tyr Asn Ile Leu 40

Met Trp Ile His Asp Asn Tyr Arg Asp Pro Glu Ser Glu Thr Asp Asn

60

55

Asp Ser Gln Glu Ile Phe Lys Leu Ala Lys Asp Val Leu Ile Gln Gly 70 75 Leu Ile Asp Glu Asn Pro Gly Leu Gln Leu Ile Ile Arg Asn Phe Trp Ser His Glu Thr Arg Leu Pro Ser Asn Thr Leu Asp Arg Leu Leu Ala Leu Asn Ser Leu Tyr Ser Pro Lys Ile Glu Val His Phe Leu Ser Leu 120 Ala Thr Asn Phe Leu Leu Glu Met Thr Ser Met Ser Pro Asp Tyr Pro 135 130 140 Asn Pro Met Phe Glu His Pro Leu Ser Glu Cys Glu Phe Gln Glu Tyr 145 150 155 Thr Ile Asp Ser Asp Trp Arg Phe Arg Ser Thr Val Leu Thr Pro Met 165 170 Phe Val Glu Thr Gln Ala Ser Gln Gly Thr Leu Gln Thr Arg Thr Gln 180 185 Glu Gly Ser Leu Ser Ala Arg Trp Pro Val Ala Gly Gln Ile Arg Ala 200 Thr Gln Gln Gln His Asp Phe Thr Leu Thr Gln Thr Ala Asp Gly Arg 215 220 210 Ser Ser Phe Asp Trp Leu Thr Gly Ser Ser Thr Asp Pro Leu Val Asp 225 230 235 His Thr Ser Pro Ser Ser Asp Ser Leu Leu Phe Ala His Lys Arg Ser 245 250 255 Glu Arg Leu Gln Arg Ala Pro Leu Lys Ser Val Gly Pro Asp Phe Gly 265

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Thr Gln Ala Ser Gln Gly Thr Leu Gln Thr Arg Thr Gln Glu Gly Ser
Leu Ser Ala Arg Trp Pro Val Ala Gly Gln Ile Arg Ala Thr Gln Gln
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Gln His Asp Phe Thr Leu Thr Gln Thr Ala Asp Gly Arg Ser Ser Phe
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Asp Trp Leu Thr Gly Ser Ser Thr Asp Pro Leu Val Asp His Thr Ser
           100
                              105
Pro Ser Ser Asp Ser Leu Leu Phe Ala His Lys Arg Ser Glu Arg Leu
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Gly Gln Ile Arg Ala Thr Gln Gln His Asp Phe Thr Leu Thr Gln
                            40
Thr Ala Asp Gly Arg Ser Ser Phe Asp Trp Leu Thr Gly Ser Ser Thr
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Asp Pro Leu Val Asp His Thr Ser Pro Ser Ser Asp Ser Leu Leu Phe
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                                                                     120
gcactaaatt ccttatattc tcctaagata gaagtgcact ttttaagttt agcaacaaat
                                                                     180
tttctgctcg aaatgaccag catgagccca gattatccaa accccatgtt cgagcatcct
                                                                     240
ctgtcagaat gcgaatttca ggaatatacc attgattctg attggcgttt ccgaagtact
                                                                     300
gttctcactc cgatgtttgt ggagacccag gcctcccagg gcactctcca gacccgtacc
                                                                     360
caggaagggt ccctctcagc tcgctqqcca qtqqcaqqqc agataagqqc cacccaqcaq
                                                                     420
cagcatgact tcacactgac acagactgca gatggaagaa gctcatttga ttggctqacc
                                                                     480
                                                                     540
gggagcagca ctgacccqct gqtcgaccac accagtccct catctgactc cttqctqttt
gcccacaaga ggagtgaaag gttacagaga gcacccttga agtcagtggg gcctgatttt
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agggaacaaa tgtataatat tctcatgtgg attcatgata attacagaga tccagaaagt
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gagacagata atgactccca ggaaatattt aagttggcaa aagatgtgct gattcaagga
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                                                                      420
ccagattatc caaaccccat gttcgagcat cctctgtcag aatgcgaatt tcaggaatat
                                                                      480
accattgatt ctgattggcg tttccgaagt actgttctca ctccgatgtt tgtggagacc
                                                                      540
caggeeteee agggeactet ceagaceegt acceaggaag ggteeetete agetegetgg
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ccagtggcag ggcagataag ggccacccag cagcagcatg acttcacact gacacagact
                                                                      660
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gcagatggaa gaagctcatt tgattggctg accgggagca gcactgaccc gctggtcgac
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gttctcactc cgatgtttgt ggagacccag gcctcccagg gcactctcca gacccgtacc
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				-		
caggaagg	gt ccctctcage	tcgctggcca	gtggcagggc	agataagggc	cacccagcag	240
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gggagcago	ca ctgacccgct	ggtcgaccac	accagtccct	catctgactc	cttgctgttt	360
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	06 NA rtificial Sequ	ience				
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<220>

<223> Reverse primer to create T2609A mutation

<400> 28

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34